PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 032810wo/Me/sto	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/13239	International filing date *(day/month/year)* 25.11.2003	Priority date *(day/month/year)* 25.11.2002
International Patent Classification (IPC) or both national classification and IPC A61K38/38		
Applicant OCTAPHARMA AG et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
17.06.2004	14.02.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Uhl, M Telephone No. +49 89 2399-8654

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/13239

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-9 as originally filed

Claims, Numbers

1-5 received on 31.01.2005 with letter of 31.01.2005

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-5
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-5
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-5
	No:	Claims	

2. Citations and explanations

see separate sheet

D1 VERON ET AL: "COMBINED COHN/CHROMATOGRAPHY PURIFICATION PROCESS FOR THE MANUFACTURING OF HIGH PURITY HUMAN ALBUMIN FROM PLASMA"1993 COLLOQUES INSERM PARIS FR VOL.227 p. 183-188

D2 DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; November 1998 (1998-11), TANAKA K ET AL: "Purification of human albumin by the combination of the method of Cohn with liquid chromatography."

D3 US-A-4 440 679 (FERNANDES PETER M ET AL) 3 April 1984 (1984-04-03)

1. The claimed method of manufacturing an albumin fraction having a reduced PKA content including an incubation step after filling for use which lasts a certain time at a certain temperature (10 days at 30-31§C or 4 weeks at 20-25°C) is novel over the prior art. D1 and D3 disclose a method where paste V (Cohn) is reconstituted, concentrated and pasteurized in bulk and in the final containers (Art.33(2) EPC).

2. However the present method differs by the further incubation step which allows to considerable lower the PK concentration. In view of this problem there was no hint in the prior art to add a final incubation step. Thus subject matter of claims 1-5 is considered to involve an inventive step (Art. 33(3) EPC).

Claims

1. A method of manufacturing an albumin enriched fraction having a reduced prekallikrein activator (PKA) content comprising the steps of:

(a) reconstitution of paste V (Cohn fractionation)

(b) performing a concentration step of the fraction obtained in step (a),

(c) heating the fraction obtained in step (b) in a range of from 50 °C to 70 °C for a sufficient time to pasteurise the fraction, ~~and~~

(d) ~~optionally~~ filling of the obtained fraction for use, and

* (e) performing an incubation step under the following conditions for 10 days at 30-32 °C or 4 weeks at 20-25 °C.

2. The method of claim 1 wherein after filling a second pasteurisation step is performed.

~~3. The method of claim 1 and/or 2 wherein an incubating step is performed.~~

~~4. The method of claim 3 wherein the incubation step is performed under the following conditions for 10 days at 30 - 32 °C or 4 weeks at 20 - 25 °C.~~

3. The method of any one of the claims 1 to 2 wherein the pasteurisation is performed for a time period of from at least 9 h at a temperature of 58 to 65 °C.

4. An albumin containing fraction having a reduced prekallikrein activator (PKA) obtainable according to the method of at least one of the claims 1 to 3.

5. The albumin of claim 4 having a PKA content of less than 12 IU/ml, preferably 10 IU/ml, wherein the PKA is determined according to European Pharmacopeia, Fourth Edition.